ZymeTx, Inc.
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August 9, 2000

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20850

Reference Docket No. 00N-1394

Dear Sirs & Madames:

I desire to speak at the public workshop being held by the FDA Division of Clinical Devices on August 14th and 15th. This workshop is entitled "Review of criteria used to determine whether specific laboratory tests are waived from certain requirements of the Clinical Laboratory Improvement Amendments of 1988 (CLIA). The announcement for this meeting was published in the Federal Register / Vol. 65, No. 141 / Friday, July 21, 2000 / Notices.

I have submitted registration and request for oral presentation to the contact person and have provided her with a copy of my planned presentation. According to the instructions given in the notice, I am also submitting written comments to the dockets via this letter. Attached is a copy of the presentation I plan to make at the public workshop.

Thank you for your assistance in this process.

Sincerely,

Lee Youngblood

Lee Youngblood, RN
Product Manager
ZymeTx, Inc.

00N-1394

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August 9, 2000

Clara Sliva
Food and Drug Administration
HFZ-440
2098 Gaither Road
Rockville, MD 20850

Dear Ms. Sliva:

Thank you for the opportunity to speak at the upcoming FDA Division of Clinical Laboratory Devices Public Workshop on waiver criteria of CLIA 1988. In my earlier e-mail message, I mentioned that both Craig Shimasaki and I would be attending this meeting and that Craig would probably speak. However, he has a schedule conflict and will not be able to arrive until late Monday evening, so I request that I speak for our company. I look forward to attending this workshop and speaking as the representative of ZymeTx, Inc.

The notice for this meeting asked that we submit a copy of our planned presentation and that we send a copy to the dockets. Attached is a written copy of our planned comments and a copy is being mailed to the address listed in the July 21st Federal Register.

I applaud the efforts of the FDA to seek input from laboratory groups, medical professional societies, patient groups, manufacturers, manufacturing associations, and other interested parties. The workshop will be a great learning experience for me. Hopefully, it will provide your agency with the information you need *"to decide whether to continue to apply the current criteria, finalize the proposed rule published by CDC in 1995, or repropose other procedures and criteria for this process."*

Again, thank you for providing this workshop and opportunity to provide input. I look forward to seeing you on August 14th.

Sincerely,

Lee Youngblood

Lee Youngblood, RN
Product Manager

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Planned Presentation
For the
Division of Clinical Devices Public Workshop
August 14-15, 2000

Review of criteria used to determine whether specific laboratory tests are waived from certain requirements of the Clinical Laboratory Improvement Amendments of 1988 (CLIA)

Planned speaker: Lee Youngblood, RN, Product Manager

Thank you for the opportunity to be here today to express the current thoughts and position of ZymeTx, Inc. related to waived status requirements.

Technology is rapidly advancing in the field of clinical laboratory science as well as many other fields. When Congress passed the Clinical Laboratory Improvement Amendments in 1988, laboratory tests were less sophisticated and much fewer in number than they are today. I understand that originally there were only a handful of tests in 8 categories that were classified as "waived". Today, there are over 700 waived tests on the market and new, simpler, more accurate technology is being developed every year.

I represent ZymeTx, Inc., a manufacturer of a rapid, point-of-care Influenza test, ZstatFlu®. We are particularly interested in the criteria used to determine whether specific tests are classified as waived from certain CLIA requirements. Our users and we would derive many benefits from obtaining waived status for our test. We would love for ZstatFlu® to be accessible to the literally thousands of physicians that treat flu patients but do not have moderately complex labs.

Influenza is the most common and most trivialized respiratory disease we face each year. Many of us have grown up hearing that it is "just the flu" but Influenza is a serious public health threat. The CDC states that "*Influenza is associated with more than 20,000 deaths nationwide and more than 100,000 hospitalizations.*" Every year, more than 90 million Americans develop flu-like illnesses!

In the past, there was little that could be done about flu. Now, for the first time in history, physicians have the right weapons to fight this killer disease. However, there are

currently no waived tests for Influenza. The major benefits of a flu test like ours becoming waived are:

1. **Improved Clinical Outcomes through definitive diagnosis** - Studies show that 60 percent of the time patients with flu see a doctor, they are misdiagnosed with a bacterial infection and are given an antibiotic. This misuse of antibiotics has contributed to the dangerous bacterial resistance to antibiotics. Under-diagnosis typically occurs early and late in the flu season when doctors aren't thinking about flu. In the peak of the flu season, over-diagnosing occurs and a serious bacterial illness can be misdiagnosed as flu and not treated correctly, which can lead to death of the patient. An accurate and early diagnosis can insure proper treatment to improve clinical outcomes.

2. **Wider Use** – Currently less than half of the primary care physicians in the US have CLIA Moderate or Highly Complex labs in their offices. Physicians with "waived" offices are reluctant to implement Influenza testing because they do not want to wait for the results. Consequently, they tend to diagnose on the basis of clinical symptoms alone, which is highly inaccurate. Waived status for flu testing would provide greater access to primary care physicians who see flu patients in their offices.

3. **Economic Impact** – A more accurate diagnosis of Influenza results in appropriate prescribing of antivirals and antibiotics in addition to avoiding unnecessary laboratory and radiological testing or expensive hospitalizations. So, it stands to reason that wider use of rapid flu diagnostics would greatly reduce global health care costs. Waived status would also allow physicians to avoid the expenses involved with using a Moderately Complex test, such as daily QC and proficiency testing which are not reimbursed by Medicare/Medicaid or third party payers.

However, we realize that such status cannot and should not be awarded to any clinical laboratory test unless the manufacturer successfully demonstrates simplicity, accuracy, reliability and safety.

SIMPLICITY – A waived test should be easy to perform and have no more than 5 simple steps. The instructions should be clearly written and easy to understand, even at the seventh grade level.

ACCURACY – A waived test should be highly accurate, even in the hands of inexperienced users. A performance level of at least 90% sensitivity and 90% specificity should be demonstrated. With many diseases, like influenza, there is too much at risk to allow widespread use of an inaccurate test.

RELIABILITY – We agree that waived tests should "render the likelihood of erroneous results by the user negligible".

SAFETY – We also agree that a waived test should "pose no unreasonable risk of harm to the patient if performed incorrectly". Therefore, if the test fails by component or user error, it should provide a mechanism of identifying such failure.

Discussion Questions:

In the notice for this meeting, several questions were specifically listed for input. Some of the questions do not apply to our particular test and I will not address those issues. However, I would like to briefly discuss those questions that do relate.

1. To demonstrate that a waived test is simple and carries "an insignificant risk of an erroneous result" we feel that a waived test should be proven as highly accurate and compared to a standard reference. In the case of flu tests, the comparison would be to viral culture. In addition, a waived test should perform equally well by trained and untrained users. We do not feel that there is a need for the FDA to apply a different model to determine the waived status of a test.

2. To determine if a methodology is "so simple and accurate to render the likelihood of erroneous results by the user negligible", we do not feel that a waived test be so accurate when performed by untrained users that inaccurate results will not occur, because there are few tests that have 100% accuracy. We also do not feel that variable accuracy criteria is acceptable (to waive tests that have inaccurate results but do not have any major negative clinical impact). We believe that all waived tests should have a high level of accuracy.

3. (Not applicable)

4. (Not applicable)

5. Accuracy should be determined using comparison of the waiver test to a well-characterized reference. Standard references for performance and accuracy are needed. However, new technologies often employ new and improved methods and materials.

6. We believe that a minimum of 100 samples should be evaluated including at least 5 users and 3 sites to evaluate accuracy.

7. The background of these users should include trained laboratorians, medical technicians, nurses and physician office personnel, and lay people (7^{th} graders).

8. We believe that the performance criteria FDA should apply to the accuracy threshold for a waived test is sensitivity and specificity both in the 90% range.

9. Concerning types of samples, how many and what types of operators/sites are appropriate, we feel that the current CDC recommendation for 20 samples at three levels seems sufficient.

10. The FDA should use percent agreement out of total repeat runs as performance thresholds to determine whether the precision studies are appropriate for waiver status.

11. (Not applicable)

12. Temperature and humidity studies would be helpful as environmental studies or flex (stress) studies to establish performance of waived tests.

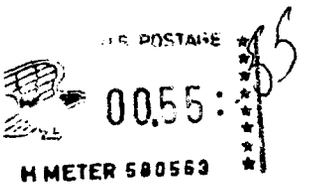
13. Ease of interpretation of results and consistency of interpretation, especially of borderline results, should be submitted for evaluation of qualitative tests for waiver.

14. Applicable threshold limits should be submitted for evaluation of quantitative tests for waiver.

Again, please let me thank you holding this workshop and allowing me this opportunity to provide input.

Lee Youngblood

Lee Youngblood, RN
Product Manager
ZymeTx, Inc.



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